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Consecutive S_NH and Suzuki–Miyaura Cross-Coupling Reactions – an Efficient Synthetic Strategy to Pyrimidines Bearing Pyrrole and Indole Fragments

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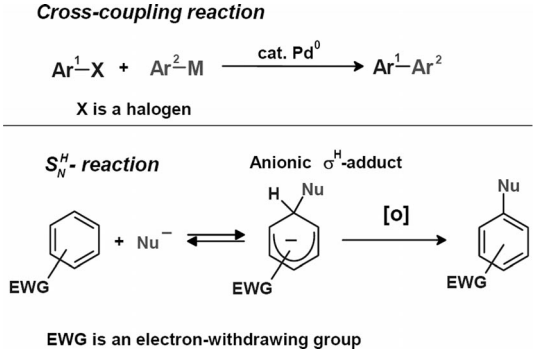
The combination of the Suzuki–Miyaura cross-coupling and nucleophilic aromatic substitution of hydrogen reactions is a versatile tool for the syntheses of 4-(1R-pyrrol-2-yl)- and 4-(1R-indol-3-yl)-5-(hetero)aryl-substituted pyrimidines from commercially available 5-bromopyrimidine. The S_NH [AE, (addition–elimination)] and S_NH [AO, (addition–oxidation)] reactions of 5-bromopyrimidine with pyrroles and indoles were studied by gas chromatography–mass spectrometry. The structures of the intermediate σ^H adducts as well as the pyrrole-(hetero)arylpyrimidine and indole-(hetero)arylpyrimidine dyads were established for the first time by X-ray crystal structure analysis.

Introduction

Transition-metal-catalyzed cross-coupling reactions are now recognized as one of the most powerful synthetic tools for carbon–carbon bond formations. The palladium-catalyzed coupling of aryl halides or their synthetic equivalents, such as aryl triflates, with aryl metal compounds (Ar–M, M = Mg, Zn, B, Sn, Si, etc.) are quite often exploited for the syntheses of biaryl molecules, whose skeletons are found in a wide range of important compounds including natural products and organic functional materials (see Scheme 1).[1–3] In particular, the Suzuki–Miyaura cross-coupling reactions of aryl halides with organoboronic acids [M = $B(OH)_2$] proved to be a versatile approach for the selective formation of carbon–carbon bonds.[4]

Another synthetic methodology to form the C–C and C–X (X is a heteroatom) bonds is based on the nucleophilic aromatic substitution of hydrogen (S_NH, see Scheme 1).[5] The advantage of this approach is that it requires neither the presence of a halogen atom in the aromatic substrate nor an expensive metal catalyst.

Pyrimidines belong to an important class of heteroaromatic compounds that have found wide applications as effective pharmaceuticals, agrochemicals, and organic materials.[6] A number of pyrimidines are known to exhibit hypnotic, antitumor, antiviral, and antimicrobial activities.[7] On the other hand, pyrrole and indole derivatives are part of the many natural compounds and synthetic drugs that demonstrate a wide range of biological activities.[7,8] Thus, the syntheses of polycyclic systems bearing the pyrimidine ring and pyrrole or indole substituents are of interest for medicinal chemistry. In particular, 4-(1-methyl-1*H*-pyrrol-2-yl)pyrimidine[9] and 3-(pyrimidin-4-yl)-1*H*-indole[10] are the simplest representatives of these heterocyclic systems, which were obtained previously and utilized for further transformations. However, it should be noted that general synthetic methods enabling one to modify the aryl substituents on the pyrimidine core have not been described in the literature.



Scheme 1.

In this communication, we report a new and convenient approach to (pyrrol-2-yl)- and (indol-3-yl)-substituted pyrimidines by using a combination of two C–C coupling reactions, that is, the microwave-assisted palladium-catalyzed Suzuki–Miyaura cross-coupling reaction and the nucleophilic aromatic substitution of hydrogen.

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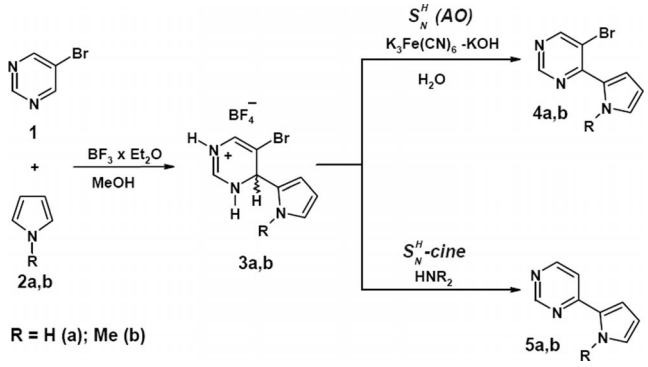
Results and Discussion

It has previously been shown that pyrimidine, 5-methylpyrimidine, and their benzannulated analogs react with a number of aromatic compounds, such as phenols, pyrroles, indoles, and thiophenes, in the presence of trifluoroacetic acid to form rather stable 4-aryl-substituted 3,4-dihydropyrimidinium salts.[11] In addition, we have used the combination of the Suzuki-Miyaura cross-coupling reaction and nucleophilic aromatic substitution of hydrogen (S_NH) in the synthesis of a series of 4,5-di(thiophen-2-yl)-substituted pyrimidines.[12]

It has been established that the reactions of pyrrole and indole derivatives with 5-bromopyrimidine (**1**) in CF_3COOH lead to rather complex multicomponent mixtures (on the basis of TLC and GC–MS data). However, the use of boron trifluoride diethyl etherate ($BF_3{\cdot}Et_2O$) as a Lewis acid in the reactions of **1** with pyrrole (**2a**) and *N*-methylpyrrole (**2b**) in methanol resulted in the formation of 5-bromo-4-(1-R-1*H*-pyrrol-2-yl)-3,4-dihydropyrimidin-1-ium tetrafluoroborates **3a** and **3b** in good yields (55–75%, see Scheme 2).



Scheme 2.

Dihydropyrimidines **3a** and **3b** appear to be intermediate σ^H adducts of the S_NH reaction and, indeed, they can be transformed into S_NH products **4** and **5**. Using $K_3Fe(CN)_6$/KOH as the oxidative system enabled us to transform dihydropyrimidines **3a** and **3b** into the products of a nucleophilic aromatic substitution of hydrogen − 5-bromo-4-(1-R-1*H*-pyrrol-2-yl)pyrimidines **4a** and **4b**. The reaction proceeded through the classic two-step "addition–oxidation" S_NH pathway (AO).[5a] On the contrary, in the presence of secondary amines, aromatization of compounds **3a** and **3b** took place, because of the elimination of HBr, thus yielding 4-(1*H*-pyrrol-2-yl)- and 4-(1-methyl-1*H*-pyrrol-2-yl)-substituted pyrimidines **5a** and **5b**, respectively, as products of the *cine* substitution of hydrogen (see Scheme 2 and Table 1). It was shown previously that the *cine* substitution of hydrogen, in the case of dihydropyrimidines, proceeds better in piperidine.[12] Using an oxidant for the S_NH *cine* substitution reactions was unnecessary, as it has been proved unambiguously that these reactions can be carried out under inert oxygen-free conditions.

Table 1. Effects of the reaction conditions on structure and yields of S_NH products **4a**, **4b**, **5a**, **5b**, **8a**, **8b**, **9a**, and **9b** derived from σ^H adducts **3a**, **3b**, **7a**, and **7b**.

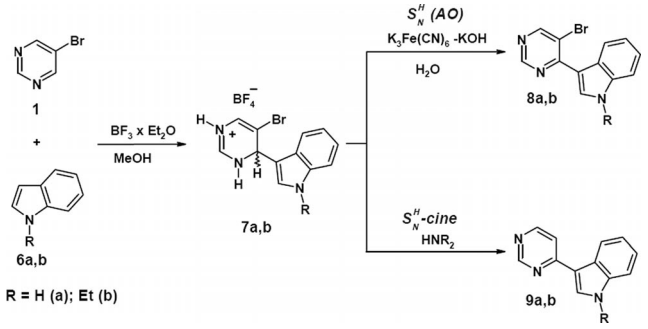
Entry	σ^H Adduct	Reaction conditions	Time [h]	S_NH product	Isol. yield [%]	Reaction mixtures [%][a]
1	**3a**	$K_3Fe(CN)_6$/KOH/H_2O	2	**4a**	50	**4a** (62) **5a** (25) impurities (13)
2	**3b**	$K_3Fe(CN)_6$/KOH/H_2O	2	**4b**	52	**4b** (76) impurities (24)
3	**3a**	piperidine	24	**5a**	25	**5a** (50) impurities (50)
4	**3b**	piperidine	24	**5b**	35	**5b** (57) **4b** (3) **3b** (6) impurities (34)
5	**7a**	$K_3Fe(CN)_6$/KOH/H_2O	2	**8a**	40	**8a** (61) **1** (8) **6a** (12) **9a** (17) impurities (2)
6	**7b**	$K_3Fe(CN)_6$/KOH/H_2O	2	**8b**	40	**8b** (59) **1** (9) **6b** (25) impurities (7)
7	**7a**	piperidine	24	**9a**	23	**9a** (37) **1** (22) **6a** (35) impurities (6)
8	**7b**	piperidine	24	**9b**	51	**9b** (63) **6b** (6) **9a** (12) impurities (19)

[a] To study the reaction mixtures, the solvent was removed by distillation, and the residue was analyzed by GC–MS.

The unequivocal evidence for the structures of the substituted dihydropyrimidines and the final S_NH products, in particular for 5-bromo-4-(1-methyl-1*H*-pyrrol-2-yl)-3,4-dihydropyrimidinium tetrafluoroborate (**3b**) and 5-bromo-4-(1*H*-pyrrol-2-yl)pyrimidine (**4a**), has been obtained by X-ray crystal structure analysis (see Supporting Information, Figures S1 and S2).

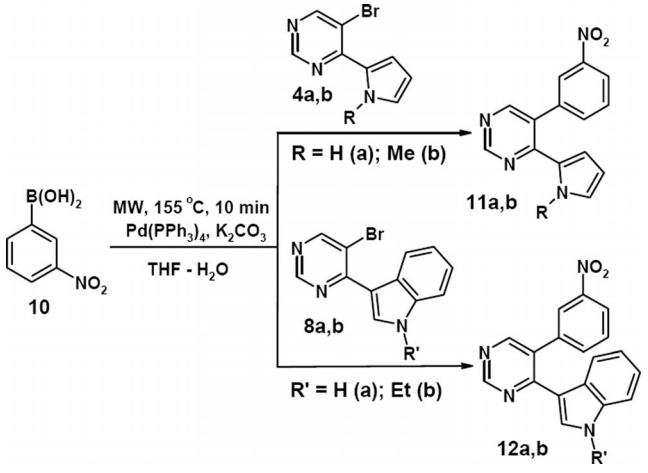
The reactions of **1** with indoles have been shown to occur in a similar manner. Indeed, in methanol, 5-bromopyrimidine (**1**) in the presence of boron trifluoride diethyl etherate ($BF_3{\cdot}Et_2O$) underwent reaction with indole (**6a**) or *N*-ethylindole (**6b**) to afford the corresponding 5-bromo-4-(1-R-1*H*-indol-3-yl)-3,4-dihydropyrimidin-1-ium tetrafluoroborates **7a** and **7b** in moderate yields (50–65%, see Scheme 3). The S_NH (AO) products, 3-(5-bromopyrimidin-4-yl)-1-R-1*H*-indoles **8a** and **8b** were obtained by using $K_3Fe(CN)_6$/KOH in water, whereas the S_NH *cine* substitution products, 1-R-3-pyrimidin-4-yl-1*H*-indoles **9a** and **9b**, were formed in the presence of piperidine (see Scheme 3 and Table 1). The

structures of the S_NH (AO) products **8a** and **8b** were confirmed by X-ray crystal structure analysis (see Supporting Information, Figures S3 and S4).



Scheme 3.

The bromo compounds **4a**, **4b**, **8a**, and **8b** were further treated with 3-nitrophenylboronic acid (**10**) under microwave irradiation (MW, 155 °C, 10 min) in a Suzuki–Miyaura cross-coupling reaction. The reaction of pyrimidines **4b** and **8b** with boronic acid **10** resulted in the formation of 4-(1-methyl-1*H*-pyrrol-2-yl)-5-(3-nitrophenyl)pyrimidine (**11b**) and 1-ethyl-3-[5-(3-nitrophenyl)pyrimidin-4-yl]-1*H*-indole (**12b**) in good yields (see Scheme 4 and Table 2). Unfortunately, under the same conditions, the reaction of pyrimidines **4a** and **8a** with boronic acid gave the 4,5-disubstituted pyrimidines **11a** and **12a**, respectively, in only trace amounts (approximately 1%), measured by GC–MS. Compounds **11a** and **12a** were not isolated.



Scheme 4.

It is worth nothing that the described method above for obtaining 4-(pyrrole-2-yl)-5-aryl- and 4-(indol-3-yl)-5-aryl-substituted pyrimidines, **11** and **12**, respectively, is not a unique one and can be complemented with an inverted sequence of S_NH and cross-coupling reactions.

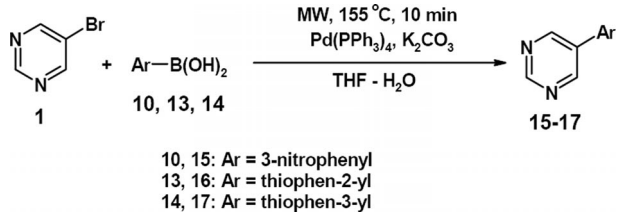
To realize this, we first obtained 5-(3-nitrophenyl)pyrimidine (**15**). In addition, to show the synthetic potential of this sequence of S_NH and cross-coupling reactions, 5-(thiophen-2-yl)pyrimidine (**16**) and 5-(thiophen-3-yl)pyrimidine (**17**) were obtained, and their reactivity in S_NH reactions

Table 2. The microwave-assisted Suzuki–Miyaura cross-coupling reaction of 5-bromo-4-aryl-substituted pyrimidines **4b** and **8b** with 3-nitrophenylboronic acid (**10**).

Entry	Pyrimidine	Isolated yield [%]	Reaction mixtures [%][a]
1	**4b**	**11b** (58)	**11b** (4) **1** (2) Ph_3PO (92) impurities (50)
2	**8b**	**12b** (70)	**12b** (15) **9b** (47) Ph_3PO (29) impurities (9)

[a] Analyzed by GC–MS.

with pyrroles **2a** and **2b** and indoles **6a** and **6b** were elucidated. Compounds **15**–**17** were obtained in high yields by using a similar cross-coupling procedure under microwave activation at 155 °C in THF (tetrahydrofuran)/H_2O (3:4, see Scheme 5).

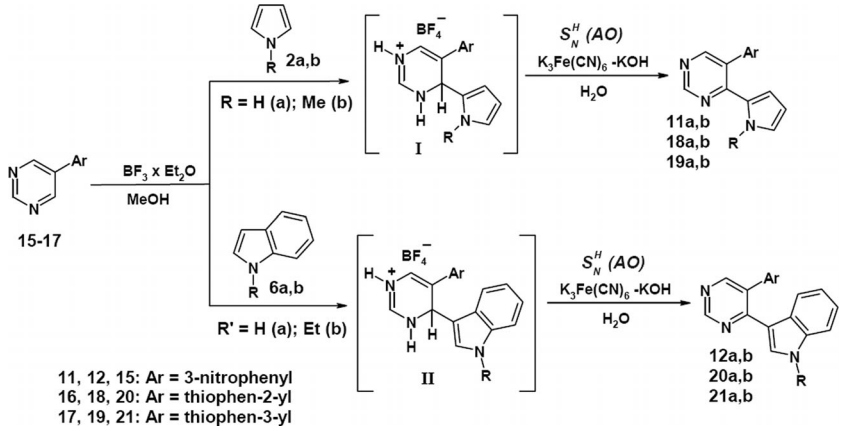


Scheme 5.

Pyrimidines **15**–**17** were then involved in the reactions with pyrroles **2a** and **2b** and indoles **6a** and **6b** in MeOH in the presence of $BF_3{\cdot}Et_2O$. The resulting reaction mixtures were stirred at room temperature for 24 h. After that time, the solvent was removed, and the corresponding 1,2-dihydropyrimidines **I** or **II**, without any further purification, were oxidized with $K_3Fe(CN)_6$ in an aqueous solution KOH for the appropriate time (see Scheme 6 and Table 3).

The reaction mixtures were analyzed by GC–MS, and the 4,5-di(hetero)aryl-substituted pyrimidines **11**, **12**, and **18**–**21** were obtained only in moderate yields, apparently, because of side reactions followed by the oxidation of intermediate σ^H adducts **I** and **II**. As the yields (GC–MS data) of 3-[5-(3-nitrophenyl)pyrimidin-4-yl]-1*H*-indole (**12a**), 3-[5-(thiophen-2-yl)pyrimidin-4-yl]-1*H*-indole (**20a**), and 3-[5-(thiophen-3-yl)pyrimidin-4-yl]-1*H*-indole (**21a**) were low (see Table 3, Entries 7, 9, and 11,), the corresponding S_NH products were not isolated. However, the structure of 4-(1*H*-pyrrol-2-yl)-5-thiophen-2-yl-pyrimidine (**18a**) was confirmed by X-ray crystal structure analysis (see Supporting Information, Figure S5).

With regard to all of the synthesized pyrrolyl-pyrimidines (i.e., **3a**, **4a**, **5a**, **11a**, **18a**, and **19a**) with an unsubstituted nitrogen in the pyrrole ring, we noted an interesting feature in their ^1H NMR spectra. The NH protons give a broadened singlet, the half linewidth of which varies from 20 to 50 Hz. Taking this into account, it is unlikely to expect the appearance of coupling between the NH proton and CH protons in the pyrrole ring. Therefore the expected



Scheme 6.

Table 3. Reaction of 5-(hetero)arylpyrimidines **15**–**17** with pyrroles **2a** and **2b** and indoles **6a** and **6b**. Composition of the reaction mixtures and yields of 4,5-di(hetero)aryl-substituted pyrimidines **11**, **12**, and **18**–**21**.

Entry	Reactants	Oxidation conditions	Time [h]	Reaction mixtures [%][a]	Isolated yield [%]
1	**15** + **2a**	room temp.	2	**11a** (39) impurities (61)	**11a** (36)
2	**15** + **2b**	room temp.	2	**11b** (59) impurities (41)	**11b** (55)
3	**16** + **2a**	room temp.	24	**18a** (69) **16** (23) impurities (8)	**18a** (42)
4	**16** + **2b**	room temp.	24	**18b** (89) impurities (11)	**18b** (38)
5	**17** + **2a**	room temp.	24	**19a** (77) **17** (13) impurities (10)	**19a** (54)
6	**17** + **2b**	room temp.	24	**19b** (68) **17** (5) impurities (27)	**19b** (51)
7	**15** + **6a**	room temp.	2	**12a** (2) **15** (46) **6a** (50) impurities (2)	**12a**[b]
8	**15** + **6b**	room temp.	24	**12b** (52) **6b** (21) impurities (27)	**12b** (33)
9	**16** + **6a**	room temp.	24	**20a** (45) **16** (21) **6a** (29) impurities (5)	**20a**[b]
10	**16** + **6b**	reflux	2	**20b** (4) **6b** (94) impurities (2)	**20b** (15)
11	**17** + **6a**	room temp.	24	**21a** (26) **17** (28) **6a** (29) impurities (17)	**21a**[b]
12	**17** + **6b**	reflux	2	**21b** (12) **6b** (80) impurities (8)	**21b** (13)

[a] Reaction mixtures analyzed by GC–MS after oxidation with $K_3Fe(CN)_6$. [b] The product was not isolated.

multiplicity of the CH proton signal should be a double doublet because of the $^3J_{H,H}$ and $^4J_{H,H}$ coupling constants. However, additional splitting from all of the pyrrole proton signals was observed in the ^1H NMR spectra of compounds **3a**, **4a**, **5a**, **11a**, **18a**, and **19a**, which was because of the coupling with the NH proton. It was confirmed by a $^1H\{^1H\}$ double-resonance experiment, in which the simplification of the splitting patterns was observed as the NH resonance was irradiated (see Figure 1). The measured values of the coupling constants turned out to be approximately the same, that is, $^4J_{NH,H(3')} \approx {}^4J_{NH,H(4')} \approx {}^3J_{NH,H(5')}$, and were in the range of 2.5–2.7 Hz.

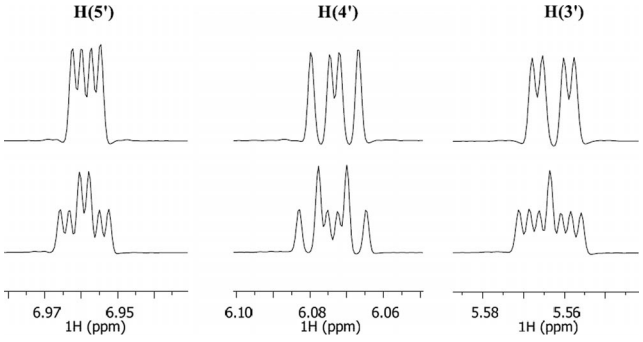


Figure 1. Multiplets of the pyrrole protons in the ^1H NMR spectrum (500 MHz, $CDCl_3$) of compound **11a**. The regular (bottom) and the NH decoupled (top) spectra.

Conclusions

The tandem cross-coupling and S_NH reactions have been shown to be a versatile tool for the syntheses of pyrimidines bearing pyrrole and indole fragments. The X-ray crystal structure data for a number of bromo- and (hetero)aryl-substituted pyrimidines provide unequivocal evidence for the suggested structures.

Experimental Section

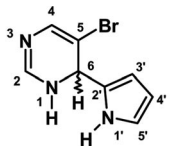
General Methods: The solvents and reagents were dried and purified according to the described procedures.[13]The starting 5-bromopyrimidine (**1**), pyrrole (**2a**), *N*-methylpyrrole (**2b**), and indole (**6a**) were purchased from Sigma–Aldrich and used without ad-

ditional purification. *N*-Ethylindole was prepared according to a reported method.[14] The solvents (THF and H_2O) used for the microwave-assisted Suzuki cross-coupling reaction were deoxygenated by bubbling argon through them for 1 h. ^1H and ^{13}C NMR spectroscopic data were recorded with Bruker DRX-400 and AVANCE-500 instruments, using Me_4Si as an internal standard. All of the signals in the ^1H and ^{13}C NMR spectra were assigned on the basis of 2D ^1H–^1H COSY, ^1H–^{13}C HSQC (heteronuclear single quantum correlation), and HMBC experiments. Elemental analyses were carried with a Eurovector EA 3000 automated analyzer. Melting points were measured using a Boetius with combined heating stages. The GC–MS analyses of all of the samples were carried out with an Agilent GC 7890A MS 5975C Inert XL EI/CI GC–MS spectrometer, using a quadrupole mass spectrometric detector with electron ionization (70 eV) and a quartz capillary column HP-5MS (30 m × 0.25 mm, film thickness, 0.25 mm), and scanned over the total ionic current in the range *m*/*z* 20–1000. Helium served as the carrier gas, and the split ratio of the flow was 1:50. The consumption through the column was 1.0 mL min^{-1}. The initial temperature of the column was 40 °C (storage 3 min), and the programming rate was 10 °C min^{-1} to 290 °C (storage 20 min). The temperatures of the evaporator and the source were 250 and 230 °C, respectively, and the temperatures of the quadrupole and the transition chamber were 150 and 280 °C, respectively. Solutions of the samples were prepared in acetonitrile with a concentration of 3–4 mg mL^{-1}, and 1-mL samples of the obtained solutions were analyzed. Column chromatography was carried out using Lancaster silica gel 0.040–0.063 mm (230–400 mesh), eluting with ethyl acetate/hexane (1:2). The progress of reactions and the purity of compounds were checked by TLC on Sorbfil plates (Russia), and the spots were visualized by UV light (λ = 254 or 365 nm). Microwave experiments were carried out with a Discover unimodal microwave system (CEM, USA) with a working frequency of 2.45 GHz, and the power of the microwave radiation ranged from 0 to 300 W. The reactions were carried out in a 10-mL reaction tube with a hermetic Teflon® stopper. The temperature of the reaction was monitored using an IR sensor inserted through the external surface of the reaction vessel. X-Ray crystal structure data were collected with an Xcalibur CCD diffractometer, using Mo-K_α (λ = 0.71069 Å) radiation at T = 295(2) K. The crystal data and data collection parameters are summarized in Table S4 (see Supporting Information). Unit cell parameters were refined using all of the collected spots after the integration process. The details of the refinement and the final R indices are presented in Table S4.

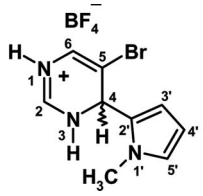
CCDC-881598 (for **3b**), -881597 (for **4a**), -881599 (for **8a**), -881600 (for **8b**), and -881601 (for **18a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Syntheses of the σ^H Adducts

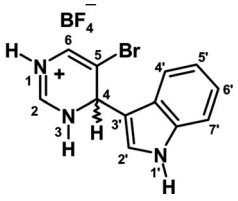
5-Bromo-4-(1-R-1*H*-pyrrol-2-yl)-3,4-dihydropyrimidin-1-iums and 5-Bromo-4-(1-R-1*H*-indol-3-yl)-3,4-dihydropyrimidin-1-iums Tetrafluoroborates 3a, 3b, 7a, and 7b: To a stirred mixture of 5-bromopyrimidine (**1**, 159 mg, 2.0 mmol) and compound **2a**, **2b**, **6a**, or **6b** (2.0 mmol) in MeOH (3 mL) was added BF_3·Et_2O (1.1 mmol). The reaction mixture was stirred at room temperature for 24 h, and the solvent was evaporated. In general, after removal of the solvent under reduced pressure, the residue was washed with ethyl acetate or Et_2O and then with $CHCl_3$. However, in the case of compound **3a**, the residue was preliminarily washed with aqueous Na_2CO_3 and then with MeCN.



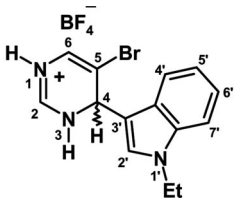
5-Bromo-4-(1*H*-pyrrol-2-yl)-3,4-dihydropyrimidine (3a): Pale green crystalline powder (122 mg, 54%); m.p. 141–142 °C (decomp). ^1H NMR (500 MHz, CD_3CN): δ = 5.28 (s, 1 H, 6-H), 6.02–6.04 (m, 2 H, 4′-H and 3′-H), 6.3–6.9 (br. s, NH, H_2O) 6.56 (s, 1 H, 4-H), 6.69 (td, J = 2.6, 1.7 Hz, 1 H, 5′-H), 7.01 (s, 1 H, 2-H), 9.24 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, CD_3CN): δ = 57.08, 102.03 (br. s), 107.82, 109.23, 119.43, 131.26 (br. s), 135.08, 144.87 ppm. $C_8H_8BrN_3$ (226.08): calcd. C 42.50, H 3.57, N 18.59, Br 35.34; found C 42.55, H 3.43, N 18.49, Br 35.53.



5-Bromo-4-(1-methyl-1*H*-pyrrol-2-yl)-3,4-dihydropyrimidin-1-ium Tetrafluoroborate (3b): Pale yellow powder (239 mg, 73%); m.p. 143–145 °C. ^1H NMR (500 MHz, CD_3CN): δ = 3.66 (s, 3 H, NCH_3), 5.66 (s, 1 H, 4-H), 6.09 (dd, J = 3.7, 2.9 Hz, 1 H, 4′-H), 6.25 (dd, J = 3.7, 1.8 Hz, 1 H, 3′-H), 6.72 (t, J = 2.3 Hz, 1 H, 5′-H), 6.75 (s, 1 H, 6-H), 7.91 (s, 1 H, 2-H), 8.41 (br. s, 2 H, NH-3 and NH-1) ppm. ^{13}C NMR (126 MHz, CD_3CN): δ = 34.96 (NCH_3), 53.23 (C-4), 106.62 (C-5), 109.19 (C-4′), 112.95 (C-3′), 122.83 (C-6), 126.61 (C-5′), 130.76 (C-2′), 148.62 (C-2) ppm. $C_9H_{11}BBrF_4N_3$ (327.92): calcd. C 32.97, H 3.38, N 12.81; found C 33.00, H 3.24, N 12.79.

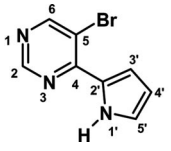


5-Bromo-4-(1*H*-indol-3-yl)-3,4-dihydropyrimidin-1-ium Tetrafluoroborate (7a): Dark red oil (240 mg, 66%). ^1H NMR (500 MHz, CD_3CN): δ = 5.81 (dd, J = 1.9, 1.1 Hz, 1 H, 4-H), 6.76 (dm, J = 4.8 Hz, 1 H, 6-H), 7.15 (ddd, J = 8.0, 7.0, 1.1 Hz, 1 H, 5′-H), 7.22 (ddd, J = 8.1, 7.0, 1.2 Hz, 1 H, 6′-H), 7.43 (d, J = 2.7 Hz, 1 H, 2′-H), 7.52 (dm, J = 8.1 Hz, 1 H, 7′-H), 7.58 (dm, J = 8.0 Hz, 1 H, 4′-H), 7.95 (t, J = 5.8 Hz, 1 H, 2-H), 8.58 (br. s, 1 H, NH-3), 9.27 (br. s, 1 H, NH-1), 9.67 (br. s, 1 H, NH-1′) ppm. ^{13}C NMR (126 MHz, CD_3CN): δ = 54.64 (C-4), 107.68 (C-5), 113.86 (C-7′), 114.23 (C-3′), 119.59 (C-4′), 121.82 (C-5′), 122.72 (C-6), 124.02 (C-6′), 126.22 (C-3′a), 127.8 (C-2′), 138.31 (C-7′a), 148.8 (C-2) ppm. $C_{12}H_{11}BBrF_4N_3$ (363.95): calcd. C 39.60, H 3.05, N 11.55; found C 39.97, H 2.27, N 11.57.

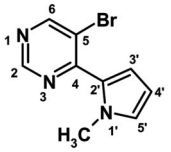


5-Bromo-4-(1-ethyl-1*H*-indol-3-yl)-3,4-dihydropyrimidin-1-ium Tetrafluoroborate (7b): Pink powder (188 mg, 48%); m.p. 162–163 °C. ^{1}H NMR (500 MHz, CD_3CN): δ = 1.42 (t, J = 7.2 Hz, 3 H, CH_3), 4.22 (q, J = 7.2 Hz, 2 H, NCH_2), 5.84 (d, J = 1.0 Hz, 1 H, 4-H), 6.79 (s, 1 H, 6-H), 7.17 (ddd, J = 8.0, 7.1, 1.1 Hz, 1 H, 5′-H), 7.28 (ddd, J = 8.2, 7.1, 1.1 Hz, 1 H, 6′-H), 7.45 (s, 1 H, 2′-H), 7.50 (dm, J = 8.2 Hz, 1 H, 7′-H), 7.58 (dm, J = 8.0 Hz, 1 H, 4′-H), 7.95 (s, 1 H, 2-H), 8.53 (br. s, 1 H, NH), 9.19 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, CD_3CN): δ = 16.16 (CH_3), 42.44 (NCH_2), 54.55 (C-4), 107.71 (C-5), 112.02 (C-7′), 113.47 (C-3′), 119.95 (C-4′), 121.72 (C-5′), 122.68 (C-6), 123.78 (C-6′), 126.99 (C-3′a), 130.30 (C-2′), 138.02 (C-7′a), 148.79 (C-2) ppm. $C_{14}H_{15}BBrF_4N_3$ (392.00): calcd. C 42.90, H 3.86, N 10.72; found C 43.10, H 3.73, N 10.63.

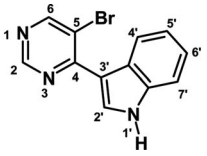
General Procedure for the Syntheses of 5-Bromo-4-(hetero)aryl-Substituted Pyrimidines 4a, 4b, 8a, and 8b: Compound **3a**, **3b**, **7a**, or **7b** (0.5 mmol) was added to solution of KOH (112 mg, 2.0 mmol, 4 equiv.) and $K_3Fe(CN)_6$ (329 mg, 1.0 mmol, 2 equiv.) in water (5 mL). The resulting mixture was stirred at room temperature for 2 h. The precipitate was removed by filtration, washed with H_2O, and then air dried. The residue was purified by flash column chromatography (hexane/ethyl acetate, 1:2) to afford the desired S_N^H product **4a**, **4b**, **8a**, or **8b**.



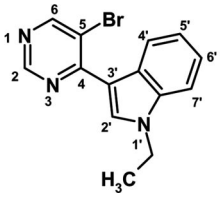
5-Bromo-4-(1*H*-pyrrol-2-yl)pyrimidine (4a): See Table 1, Entry 1. Pale yellow powder; m.p. 146–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.41 (dt, J = 3.9, 2.7 Hz, 1 H, 4′-H), 7.08 (td, J = 2.7, 1.3 Hz, 1 H, 5′-H), 7.65 (ddd, J = 3.9, 2.7, 1.3 Hz, 1 H, 3′-H), 8.73 (s, 1 H, 6-H), 8.90 (s, 1 H, 2-H), 10.00 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 112.45 (C-4′), 114.75 (C-5), 117.30 (C-3′), 123.70 (C-5′), 128.41 (C-2′), 154.28 (C-4), 156.78 (C-2), 160.97 (C-6) ppm. $C_8H_6BrN_3$ (224.06): calcd. C 42.89, H 2.70, N 18.75; found C 42.75, H 2.55, N 18.84. GC: t_R = 18.81 min. MS: m/z (%) = 223 (100) $[M]^+$ for ^{79}Br, 225 (100) $[M]^+$ for ^{81}Br.



5-Bromo-4-(1-metyl-1*H*-pyrrol-2-yl)pyrimidine (4b): See Table 1, Entry 2. White crystalline powder; m.p. 41–43 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.92 (s, 3 H, NCH_3), 6.25 (dd, J = 4.0, 2.6 Hz, 1 H, 4′-H), 6.85 (dd, J = 2.6, 1.7 Hz, 1 H, 5′-H), 7.23 (dd, J = 4.0, 1.7 Hz, 1 H, 3′-H), 8.82 (s, 1 H, 6-H), 9.01 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 38.03 (NCH_3), 108.74 (C-4′), 118.15 (C-5), 118.34 (C-3′), 128.25 (C-2′), 129.67 (C-5′), 156.64 (C-2), 157.18 (C-4), 160.82 (C-6) ppm. $C_9H_8BrN_3$ (238.09): calcd. C 45.40, H 3.39, N 17.65; found C 45.20, H 3.31, N 17.68. GC: t_R = 18.79 min. MS: m/z (%) = 237 (100) $[M]^+$ for ^{79}Br, 239 (100) $[M]^+$ for ^{81}Br.

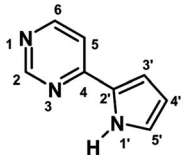


3-(5-Bromopyrimidin-4-yl)-1*H*-indole (8a): See Table 1, Entry 5. Pale beige powder; m.p. 238–240 °C. ^{1}H NMR (400 MHz, CD_3CN): δ = 7.22–7.30 (m, 2 H, 5′-H and 6′-H), 7.55 (dm, J = 8.0 Hz, 1 H, 7′-H), 8.52 (dm, J = 8.0 Hz, 1 H, 4′-H), 8.59 (d, J = 3.1 Hz, 1 H, 2′-H), 8.84 (s, 1 H, 6-H), 9.07 (s, 1 H, 2-H), 9.96 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, CD_3CN): δ = 113.31 (C-7′), 113.57 (C-3′), 117.88 (C-5), 122.72 (C-5′), 124.03 (C-4′), 124.46 (C-6′), 127.91 (C-3′a), 132.24 (C-2′), 137.72 (C-7′a), 157.74 (C-2), 161.05 (C-6), 161.08 (C-4) ppm. $C_{12}H_8BrN_3$ (274.12): calcd. C 52.58, H 2.94, N 15.33; found C 52.55, H 3.03, N 15.49. GC: t_R = 26.38 min. MS: m/z (%) = 273 (100) $[M]^+$ for ^{79}Br, 275 (100) $[M]^+$ for ^{81}Br.



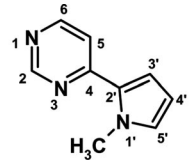
3-(5-Bromopyrimidin-4-yl)-1-ethyl-1*H*-indole (8b): See Table 1, Entry 6. Pale yellow crystalline powder; m.p. 71–72 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.54 (t, J = 7.3 Hz, 3 H, CH_3), 4.26 (q, J = 7.3 Hz, 2 H, NCH_2), 7.27–7.33 (m, 2 H, 5′-H and 6′-H), 7.40 (dm, J = 8.0 Hz, 1 H, 7′-H), 8.43 (s, 1 H, 2′-H), 8.60 (dm, J = 8.0 Hz, 1 H, 4′-H), 8.78 (s, 1 H, 6-H), 9.11 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.22 (CH_3), 41.69 (NCH_2), 109.62 (C-7′), 111.60 (C-3′), 116.45 (C-5), 121.73 (C-5′), 122.99 (C-6′), 123.14 (C-4′), 127.33 (C-3′a), 132.32 (C-2′), 136.01 (C-7′a), 156.31 (C-2), 159.34 (C-6), 159.53 (C-4) ppm. $C_{14}H_{12}BrN_3$ (302.18): calcd. C 55.65, H 4.00, N 13.91; found C 55.39, H 4.00, N 13.74. GC: t_R = 26.11 min. MS: m/z (%) = 301 (100) $[M]^+$ for ^{79}Br, 303 (100) $[M]^+$ for ^{81}Br.

General Procedure for the Syntheses of 4-(Hetero)aryl-Substituted Pyrimidines 5a, 5b, 9a, and 9b: Compound **3a**, **3b**, **7a**, or **7b** (0.5 mmol) was dissolved in piperidine (5 mL). The resulting solution was stirred at room temperature for 24 h. The solvent was removed by distillation under reduced pressure, and the residue was purified by flash column chromatography (hexane/ethyl acetate, 1:2) to afford the desired S_N^H *cine* product **5a**, **5b**, **9a**, or **9b**.

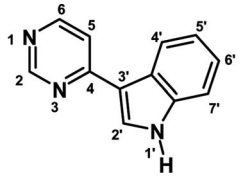


4-(1*H*-Pyrrol-2-yl)pyrimidine (5a): See Table 1, Entry 3. Pale beige crystalline powder; m.p. 116–118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.35 (dt, J = 3.7, 2.7 Hz, 1 H, 4′-H), 6.90 (ddd, J = 3.7, 2.5, 1.3 Hz, 1 H, 3′-H), 7.01 (td, J = 2.7, 1.3 Hz, 1 H, 5′-H), 7.42 (dd, J = 5.5, 1.4 Hz, 1 H, 5-H), 8.56 (d, J = 5.5 Hz, 1 H, 6-H), 9.01 (d, J = 1.4 Hz, 1 H, 2-H), 9.76 (br. s, 1 H, NH) ppm. ^{13}C NMR

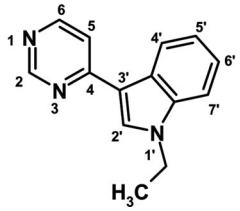
(126 MHz, $CDCl_3$): δ = 111.06 (C-3′), 111.27 (C-4′), 114.44 (C-5), 122.22 (C-5′), 129.04 (C-2′), 156.18 (C-4), 156.44 (C-6), 158.63 (C-2) ppm. $C_8H_7N_3$ (145.17): calcd. C 66.19, H 4.86, N 28.95; found C 65.96, H 4.79, N 28.76. GC: t_R = 15.82 min. MS: *m*/*z* (%) = 145 (100) $[M]^+$.



4-(1-Methyl-1*H*-pyrrol-2-yl)pyrimidine (5b): See Table 1, Entry 4. Pale yellow powder; m.p. 74–76 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.09 (s, 3 H, NCH_3), 6.21 (dd, *J* = 3.9, 2.5 Hz, 1 H, 4′-H), 6.81 (dd, *J* = 2.5, 1.8 Hz, 1 H, 5′-H), 6.84 (dd, *J* = 3.9, 1.8 Hz, 1 H, 3′-H), 7.45 (dd, *J* = 5.6, 1.3 Hz, 1 H, 5-H), 8.54 (d, *J* = 5.6 Hz, 1 H, 6-H), 9.06 (d, *J* = 1.3 Hz, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 37.97 (NCH_3), 108.55 (C-4′), 114.16 (C-3′), 116.67 (C-5), 129.12 (C-2′), 129.37 (C-5′), 156.02 (C-6), 158.17 (C-2), 158.46 (C-4) ppm. $C_9H_9N_3$ (159.19): calcd. C 67.91, H 5.70, N 26.40; found C 67.86, H 5.60, N 26.46. GC: t_R = 16.42 min. MS: *m*/*z* (%) = 159 (100) $[M]^+$.

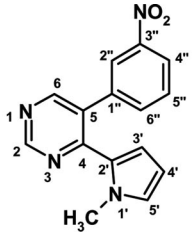


3-(Pyrimidin-4-yl)-1*H*-indole (9a):[10] See Table 1, Entry 7. Beige powder; m.p. 166–168 °C (decomp); ref.[10a] m.p. 165 °C. ^1H NMR (400 MHz, CD_3CN): δ = 7.29–7.34 (m, 2 H, 5′-H and 6′-H), 7.47 (m, 1 H, 7′-H), 7.65 (dd, *J* = 5.4, 1.4 Hz, 1 H, 5-H), 8.02 (d, *J* = 2.9 Hz, 1 H, 2′-H), 8.41 (m, 1 H, 4′-H), 8.64 (d, *J* = 5.4 Hz, 1 H, 6-H), 8.69 (br. s, 1 H, NH), 9.19 (d, *J* = 1.4 Hz, 1 H, 2-H) ppm. $C_{12}H_9N_3$ (195.23): calcd. C 73.83, H 4.65, N 21.52; found C 73.75, H 4.53, N 21.72. GC: t_R = 24.63 min. MS: *m*/*z* (%) = 195 (100) $[M]^+$.

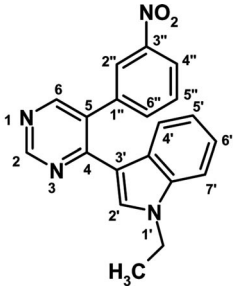


1-Ethyl-3-(pyrimidin-4-yl)-1*H*-indole (9b): See Table 1, Entry 8. Red powder; m.p. 92–94 °C. ^1H NMR (400 MHz, CD_3CN): δ = 1.40 (t, *J* = 7.2 Hz, 3 H, CH_3), 4.20 (q, *J* = 7.2 Hz, 2 H, NCH_2), 7.16–7.24 (m, 2 H, 5′-H and 6′-H), 7.44 (dm, *J* = 8.0 Hz, 1 H, 7′-H), 7.61 (dd, *J* = 5.5, 1.4 Hz, 1 H, 5-H), 8.05 (s, 1 H, 2′-H), 8.41 (dm, *J* = 8.0 Hz, 1 H, 4′-H), 8.49 (d, *J* = 5.5 Hz, 1 H, 6-H), 8.98 (d, *J* = 1.4 Hz, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.20 (CH_3), 41.53 (NCH_2), 110.04 (C-7′), 113.41 (C-3′), 116.12 (C-5), 121.44 and 121.54 (C-4′ and C-5′), 122.67 (C-6′), 125.96 (C-3′a), 129.85 (C-2′), 137.08 (C-7′a), 156.03 (C-6), 158.77 (C-2), 161.54 (C-4) ppm. $C_{14}H_{13}N_3$ (223.28): calcd. C 75.31, H 5.87, N 18.82; found C 75.52, H 5.88, N 18.60. GC: t_R = 24.61 min. MS: *m*/*z* (%) = 223 (100) $[M]^+$.

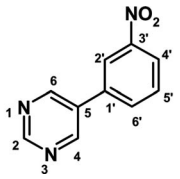
General Procedure for the Microwave-Assisted Suzuki Cross-Coupling Reactions: A solution of K_2CO_3 (346 mg, 2.5 mmol) in H_2O (4 mL) was added to a mixture of bromo-substituted pyrimidine **1**, **4b**, or **8b** (1.0 mmol), the corresponding arylboronic acid **10**, **13**, or **14** (1.2 mmol), and $Pd(PPh_3)_4$ (58 mg, 5 mol-%) in THF (3 mL). The resulting mixture was deaerated by bubbling argon through it and then irradiated in a microwave apparatus at 155 °C (250 W) for 10 min. That solvent was then removed under reduced pressure, and the residue was purified by flash column chromatography (hexane/ethyl acetate, 1:2) to afford the desired cross-coupling product **11b**, **12b**, **15**, **16**, or **17**.



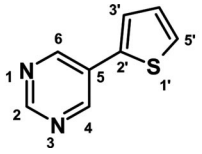
4-(1-Methyl-1*H*-pyrrol-2-yl)-5-(3-nitrophenyl)pyrimidine (11b): See Table 2, Entry 1. Yellow powder; m.p. 105–107 °C. ^1H NMR (500 MHz, [D_6]DMSO): δ = 3.88 (s, 3 H, NCH_3), 5.64 (dd, *J* = 3.9, 1.7 Hz, 1 H, 3′-H), 5.90 (dd, *J* = 3.9, 2.6 Hz, 1 H, 4′-H), 6.95 (dd, *J* = 2.6, 1.7 Hz, 1 H, 5′-H), 7.70 (td, *J* = 7.8, 0.8 Hz, 1 H, 5′′-H), 7.82 (dt, *J* = 7.6, 1.4 Hz, 1 H, 6′′-H), 8.24 (dd, *J* = 2.4, 1.6 Hz, 1 H, 2′′-H), 8.26 (ddd, *J* = 7.9, 2.4, 1.2 Hz, 1 H, 4′′-H), 8.73 (s, 1 H, 6-H), 9.18 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, [D_6]DMSO): δ = 36.30 (NCH_3), 107.75 (C-4′), 116.05 (C-3′), 122.88 (C-4′′), 123.80 (C-2′′), 127.58 (C-2′), 127.97 (C-5′), 129.91 (C-5), 130.14 (C-5′′), 136.04 (C-6′′), 138.62 (C-1′′), 147.98 (C-3′′), 155.82 (C-4), 157.17 (C-2), 157.55 (C-6) ppm. $C_{15}H_{12}N_4O_2$ (280.29): calcd. C 64.28, H 4.32, N 19.99; found C 64.21, H 4.25, N 19.96. GC: t_R = 26.07 min. MS: *m*/*z* (%) = 280 (100) $[M]^+$.



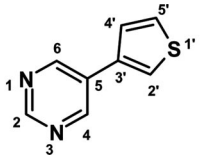
1-Ethyl-3-[5-(3-nitrophenyl)pyrimidin-4-yl]-1*H*-indole (12b): See Table 2, Entry 2. Dark yellow powder; m.p. 150–152 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.3 Hz, 3 H, CH_3), 4.01 (q, *J* = 7.3 Hz, 2 H, NCH_2), 6.72 (s, 1 H, 2′-H), 7.20 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1 H, 5′-H), 7.26 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1 H, 6′-H), 7.31 (dm, *J* = 8.1 Hz, 1 H, 7′-H), 7.58 (t, *J* = 7.9 Hz, 1 H, 5′′-H), 7.72 (dt, *J* = 7.7, 1.4 Hz, 1 H, 6′′-H), 8.24 (dm, *J* = 8.0 Hz, 1 H, 4′-H), 8.27 (ddd, *J* = 8.2, 2.2, 1.1 Hz, 1 H, 4′′-H), 8.30 (t, *J* = 1.9 Hz, 1 H, 2′-H), 8.57 (s, 1 H, 6-H), 9.25 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.14 (CH_3), 41.29 (NCH_2), 109.61 (C-7′), 111.92 (C-3′), 121.55 (C-5′), 122.39 (C-4′), 122.94 (C-6′), 123.05 (C-4′′), 124.10 (C-2′′), 126.61 (C-3′a), 129.23 (C-5), 129.97 (C-5′′), 131.09 (C-2′), 135.52 (C-6′′), 136.16 (C-7′a), 139.57 (C-1′′), 148.77 (C-3′′), 156.81 (C-6), 158.17 (C-2), 159.71 (C-4) ppm. $C_{20}H_{16}N_4O_2$ (344.38): calcd. C 69.76, H 4.68, N 16.27; found C 69.60, H 4.46, N 16.23. GC: t_R = 32.42 min. MS: *m*/*z* (%) = 344 (100) $[M]^+$.



5-(3-Nitrophenyl)pyrimidine (15): Pale yellow powder (165 mg, 82%); m.p. 158–160 °C. ^{1}H NMR (400 MHz, CD_3CN): δ = 7.78 (t, J = 8.0 Hz, 1 H, 5′-H), 8.09 (ddd, J = 7.7, 1.9, 1.0 Hz, 1 H, 6′-H), 8.31 (ddd, J = 8.2, 2.3, 1.0 Hz, 1 H, 4′-H), 8.54 (t, J = 2.0 Hz, 1 H, 2′-H), 9.08 (s, 2 H, 4-H and 6-H), 9.21 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, CD_3CN): δ = 123.35 (C-2′), 124.97 (C-4′), 132.05 (C-5′), 133.50 (C-5), 134.84 (C-6′), 137.69 (C-1′), 150.46 (C-3′), 156.68 (C-4 and C-6), 159.62 (C-2) ppm. $C_{10}H_7N_3O_2$ (201.19): calcd. C 59.70, H 3.51, N 20.89; found C 59.74, H 3.60, N 20.64. GC: t_R = 21.01 min. MS: m/z (%) = 201 (100) $[M]^+$.

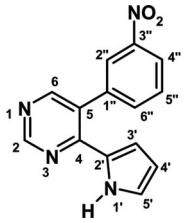


5-(Thiophen-2-yl)pyrimidine (16):[12] Pale yellow powder (105 mg, 65%); m.p. 77–78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (dd, J = 5.0, 3.6 Hz, 1 H, 4′-H), 7.44 (dd, J = 3.6, 1.1 Hz, 1 H, 3′-H), 7.47 (dd, J = 5.0, 1.1 Hz, 1 H, 5′-H), 8.98 (s, 2 H, 4-H and 6-H), 9.13 (s, 1 H, 2-H) ppm. $C_8H_6N_2S$ (162.21): calcd. C 59.24, H 3.73, N 17.27, S 19.77; found C 59.18, H 3.63, N 17.55, S 19.64. GC: t_R = 16.04 min. MS: m/z (%) = 162 (100) $[M]^+$.

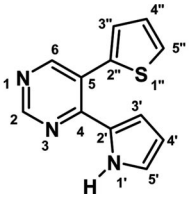


5-(Thiophen-3-yl)pyrimidine (17):[15] Pale beige powder (135 mg, 83%). M.p. 102–103 °C; ref.[15] m.p. 97–98 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41 (dd, J = 5.0, 1.4 Hz, 1 H, 4′-H), 7.51 (dd, J = 5.0, 3.0 Hz, 1 H, 5′-H), 7.61 (dd, J = 3.0, 1.4 Hz 1 H, 2′-H), 8.96 (s, 2 H, 4, 6-H), 9.15 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 122.51 (C-2′), 125.34 (C-4′), 127.77 (C-5′), 129.49 (C-5), 135.06 (C-3′), 154.13 (C-4 and C-6), 157.15 (C-2) ppm. $C_8H_6N_2S$ (162.21): calcd. C 59.24, H 3.73, N 17.27, S 19.77; found C 59.28, H 3.59, N 17.47, S 19.66. GC: t_R = 16.40 min. MS: m/z (%) = 162 (100) $[M]^+$.

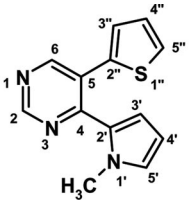
General Procedure for the Syntheses of S_NH Products – 4,5-Di-(hetero)aryl-Substituted Pyrimidines 11a, 11b, 12a, 12b, 18a, 18b–21a, and 21b: To a stirred mixture of 5-(hetero)aryl-pyrimidine **15**, **16**, or **17** (0.5 mmol) and compound **2a**, **2b**, **6a**, or **6b** (1.0 mmol) in MeOH (3 mL) was added $BF_3{\cdot}Et_2O$ (1.1 mmol). The reaction mixture was stirred at room temperature for 24 h, and the solvent was evaporated. A solution of KOH (112 mg, 2.0 mmol, 4 equiv.) and $K_3Fe(CN)_6$ (329 mg, 1.0 mmol, 2 equiv.) in water (5 mL) was added to residue. The resulting mixture was stirred for the appropriate time (see Table 3) at room temperature. The precipitate or semisolid was removed by filtration, washed with H_2O, and then air dried. The residue was purified by flash column chromatography (hexane/ethyl acetate, 1:2) to afford the desired S_NH products. However, in the case of S_NH products **20b** and **21b**, the solvent was removed under reduced pressure as above, and then the residue was dissolved in THF (3 mL). A solution of KOH (112 mg, 2.0 mmol, 4 equiv.) and $K_3Fe(CN)_6$ (329 mg, 1.0 mmol, 2 equiv.) in water (3 mL) was added, and the resulting mixture was heated at reflux for 2 h. After cooling to room temperature, the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography (hexane/ethyl acetate, 1:2) to afford the desired S_NH products **20b** or **21b**.



5-(3-Nitrophenyl)-4-(1*H*-pyrrol-2-yl)pyrimidine (11a): See Table 3, Entry 1. Yellow powder; m.p. 153–155 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.56 (ddd, J = 3.8, 2.5, 1.3 Hz, 1 H, 3′-H), 6.08 (dt, J = 3.8, 2.6 Hz, 1 H, 4′-H), 6.96 (td, J = 2.6, 1.3 Hz, 1 H, 5′-H), 7.71 (t, J = 7.8 Hz, 1 H, 5′′-H), 7.75 (dt, J = 7.6, 1.5 Hz, 1 H, 6′′-H), 8.28 (t, J = 1.9 Hz, 1 H, 2′′-H), 8.37 (ddd, J = 8.0, 2.2, 1.5 Hz, 1 H, 4′′-H), 8.42 (s, 1 H, 6-H), 9.06 (s, 1 H, 2-H), 9.99 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 111.45 (C-4′), 114.75 (C-3′), 122.20 (C-5′), 123.67 (C-4′′), 124.38 (C-2′′), 127.38 (C-5), 127.63 (C-2′), 130.20 (C-5′′), 135.56 (C-6′′), 138.43 (C-1′′), 148.75 (C-3′′), 153.54 (C-4), 157.23 (C-6), 157.83 (C-2) ppm. $C_{14}H_{10}N_4O_2$ (266.26): calcd. C 63.15, H 3.79, N 21.04; found C 63.06, H 3.76, N 20.85. GC: t_R = 26.44 min. MS: m/z (%) = 266 (100) $[M]^+$.

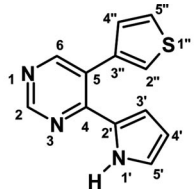


4-(1*H*-Pyrrol-2-yl)-5-(thiophen-2-yl)pyrimidine (18a): See Table 3, Entry 3. Yellow powder; m.p. 139–141 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.91 (ddd, J = 3.8, 2.5, 1.3 Hz, 1 H, 3′-H), 6.13 (dt, J = 3.8, 2.6 Hz, 1 H, 4′-H), 6.94 (td, J = 2.6, 1.3 Hz, 1 H, 5′-H), 7.14 (dd, J = 3.5, 1.2 Hz, 1 H, 3′′-H), 7.19 (dd, J = 5.1, 3.5 Hz, 1 H, 4′′-H), 7.51 (dd, J = 5.1, 1.2 Hz, 1 H, 5′′-H), 8.51 (s, 1 H, 6-H), 8.99 (s, 1 H, 2-H), 9.92 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 111.29 (C-4′), 114.69 (C-3′), 121.89 (C-5′), 122.72 (C-5), 127.26 (C-5′′), 127.75 (C-4′′), 127.84 (C-2′), 128.09 (C-3′′), 136.64 (C-2′′), 154.91 (C-4), 157.61 (C-2), 158.55 (C-6) ppm. $C_{12}H_9N_3S$ (227.29): calcd. C 63.41, H 3.99, N 18.49; found C 63.36, H 3.76, N 18.55. GC: t_R = 22.60 min. MS: m/z (%) = 227 (100) $[M]^+$.

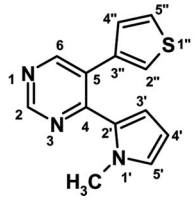


4-(1-Methyl-1*H*-pyrrol-2-yl)-(5-thiophen-2-yl)pyrimidine (18b): See Table 3, Entry 4. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.58

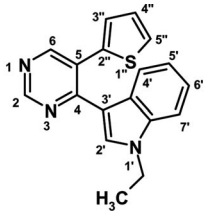
(s, 3 H, NCH_3), 6.19 (dd, J = 2.9, 1.8 Hz, 1 H, 3′-H), 6.46 (t, J = 2.6 Hz, 1 H, 4′-H), 6.87 (t, J = 2.0 Hz, 1 H, 5′-H), 7.09 (dd, J = 3.5, 1.2 Hz, 1 H, 3′′-H), 7.14 (dd, J = 5.1, 3.5 Hz, 1 H, 4′′-H), 7.46 (dd, J = 5.1, 1.2 Hz, 1 H, 5′′-H), 8.50 (s, 1 H, 6-H), 9.02 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 36.44 (NCH_3), 109.85 (C-3′), 121.64 (C-2′), 122.55 (C-4′), 123.82 (C-5), 125.49 (C-5′), 126.86 (C-5′′), 127.53 (C-4′′), 127.83 (C-3′′), 137.90 (C-2′′), 157.84 (C-2), 158.21 (C-6), 159.87 (C-4) ppm. $C_{13}H_{11}N_3S$ (241.32): calcd. C 64.71, H 4.59, N 17.41; found C 64.66, H 4.76, N 17.47. GC: t_R = 22.53 min. MS: m/z (%) = 241 (100) $[M]^+$.



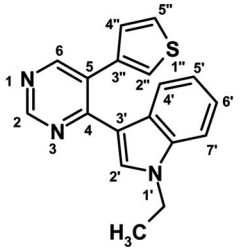
4-(1*H*-Pyrrol-2-yl)-5-(thiophen-3-yl)pyrimidine (19a): See Table 3, Entry 5. Beige powder; m.p. 140–141 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.87 (ddd, J = 3.8, 2.5, 1.3 Hz, 1 H, 3′-H), 6.13 (dt, J = 3.8, 2.6 Hz, 1 H, 4′-H), 6.94 (td, J = 2.6, 1.3 Hz, 1 H, 5′-H), 7.13 (dd, J = 5.0, 1.3 Hz, 1 H, 4′′-H), 7.35 (dd, J = 3.0, 1.3 Hz, 1 H, 2′′-H), 7.49 (dd, J = 5.0, 3.0 Hz, 1 H, 5′′-H), 8.45 (s, 1 H, 6-H), 8.99 (s, 1 H, 2-H), 9.93 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 111.14 (C-4′), 114.37 (C-3′), 121.70 (C-5′), 124.33 (C-2′′), 125.03 (C-5), 126.65 (C-5′′), 128.19 (C-2′), 128.44 (C-4′′), 136.53 (C-3′′), 154.10 (C-4), 157.12 (C-2), 157.65 (C-6) ppm. $C_{12}H_9N_3S$ (227.29): calcd. C 63.41, H 3.99, N 18.49; found C 63.56, H 4.06, N 18.66. GC: t_R = 22.83 min. MS: m/z (%) = 227 (100) $[M]^+$.



4-(1-Methyl-1*H*-pyrrol-2-yl)-5-(thiophen-3-yl)pyrimidine (19b): See Table 3, Entry 6. Pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, NCH_3), 6.02–6.05 (m, 2 H, 3′-H and 4′-H), 6.71 (t, J = 2.1 Hz, 1 H, 5′-H), 6.91 (dd, J = 5.0, 1.3 Hz, 1 H, 4′′-H), 7.26 (dd, J = 3.0, 1.3 Hz, 1 H, 2′′-H), 7.33 (dd, J = 5.0, 3.0 Hz, 1 H, 5′′-H), 8.63 (s, 1 H, 6-H), 9.08 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 36.50 (NCH_3), 108.11 (C-4′), 115.56 (C-3′), 123.64 (C-2′′), 126.22 (C-5′′), 127.24 (C-5′), 127.68 (C-5), 127.73 (C-4′′), 128.74 (C-2′), 137.08 (C-3′′), 156.26 (C-4), 156.67 (C-2), 157.19 (C-6) ppm. $C_{13}H_{11}N_3S$ (241.32): calcd. C 64.71, H 4.59, N 17.41; found C 64.57, H 4.67, N 17.35. GC: t_R = 22.82 min. MS: m/z (%) = 241 (100) $[M]^+$.



1-Ethyl-3-[5-(thiophen-2-yl)pyrimidin-4-yl]-1*H*-indole (20b): See Table 3, Entry 10. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34 (t, J = 7.3 Hz, 3 H, CH_3), 4.04 (q, J = 7.3 Hz, 2 H, NCH_2), 6.88 (s, 1 H, 2′-H), 7.10–7.13 (m, 2 H, 3′′-H and 4′′-H), 7.22 (ddd, J = 8.0, 6.8, 1.3 Hz, 1 H, 5′-H), 7.26 (ddd, J = 8.1, 6.8, 1.1 Hz, 1 H, 6′-H), 7.32 (dm, J = 8.1 Hz, 1 H, 7′-H), 7.43 (dd, J = 4.7, 2.0 Hz, 1 H, 5′′-H), 8.40 (dm, J = 8.0 Hz, 1 H, 4′-H), 8.59 (s, 1 H, 6-H), 9.17 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.04 (CH_3), 41.22 (NCH_2), 109.41 (C-7′), 111.93 (C-3′), 121.41 (C-5′), 122.54 (C-6′), 122.66 (C-4′), 124.77 (C-5), 127.04 (C-5′′), 127.09 (C-3′a), 127.64 and 127.70 (C-3′′ and C-4′′), 131.32 (C-2′), 136.04 (C-7′a), 138.44 (C-2′′), 157.45 (C-6), 157.74 (C-2), 160.78 (C-4) ppm. $C_{18}H_{15}N_3S$ (305.40): calcd. C 70.79, H 4.95, N 13.76; found C 70.66, H 5.00, N 13.69. GC: t_R = 27.90 min. MS: m/z (%) = 305 (100) $[M]^+$.



1-Ethyl-3-[5-(thiophen-3-yl)pyrimidin-4-yl]-1*H*-indole (21b): See Table 3, Entry 12. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34 (t, J = 7.3 Hz, 3 H, CH_3), 4.03 (q, J = 7.3 Hz, 2 H, NCH_2), 6.78 (s, 1 H, 2′-H), 7.01 (dd, J = 4.9, 1.4 Hz, 1 H, 4′′-H), 7.22 (ddd, J = 8.0, 6.9, 1.2 Hz, 1 H, 5′-H), 7.26 (ddd, J = 8.1, 6.9, 1.1 Hz, 1 H, 6′-H), 7.32 (dm, J = 8.1 Hz, 1 H, 7′-H), 7.36 (dd, J = 3.0, 1.4 Hz, 1 H, 2′′-H), 7.38 (dd, J = 4.9, 3.0 Hz, 1 H, 5′′-H), 8.41 (dm, J = 8.0 Hz, 1 H, 4′-H), 8.55 (s, 1 H, 6-H), 9.17 (s, 1 H, 2-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.02 (CH_3), 41.18 (NCH_2), 109.38 (C-7′), 112.31 (C-3′), 121.37 (C-5′), 122.56 (C-6′), 122.68 (C-4′), 123.92 (C-2′′), 126.51 (C-5′′), 126.79 (C-5), 127.01 (C-3′a), 128.26 (C-4′′), 131.19 (C-2′), 136.09 (C-7′a), 138.02 (C-3′′), 156.70 (C-6), 157.43 (C-2), 160.13 (C-4) ppm. $C_{18}H_{15}N_3S$ (305.40): calcd. C 70.79, H 4.95, N 13.76; found C 70.87, H 4.77, N 13.90. GC: t_R = 29.34 min. MS: m/z (%) = 305 (100) $[M]^+$.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra of the new compounds. Detailed information in Table S4 concerning crystal structures of compounds **3b**, **4a**, **8a**, **8b**, and **18a** provided by X-ray analysis.

Acknowledgments

This work was supported by the Ural Branch of the Russian Academy of Sciences (grants numbers 12-P-3-1014, 12-P-3-1030, 12-T-3-1025, and 12-T-3-1031), the State Program for Supporting of Leading Scientific Schools of the Russian Federation (grant number NSh 5505.2012.3), and the Russian Foundation for Basic Research (grant numbers 10-03-96078-r_ural_a and 12-03-31574).

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